

1 CHAIRPERSON CANADY: Could we then  
2 rephrase that, further analysis of existing data for  
3 completion purposes?

4 DR. EDMONDSON: A rhetorical question.  
5 And what if it can't be answered?

6 CHAIRPERSON CANADY: Then that decision  
7 will be made.

8 DR. PIANTADOSI: I have a rhetorical  
9 answer.

10 (Laughter.)

11 I am totally confident that the Agency has  
12 heard the concerns and that they will make an  
13 appropriate decision with the additional analyses and  
14 data clean up.

15 CHAIRPERSON CANADY: Any other comments  
16 regarding that amendment?

17 DR. NUWER: Well, I have a concern that  
18 it's a whole unforeseen set of circumstances that could  
19 arise if the company gives data of a certain sort and  
20 then that leads to further concerns and it sort of  
21 rolls on month after month and this gets stretched out  
22 for a long time without any sense of closure to it.

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1 DR. ZAMORANO: Well, basically, we have  
2 said that somehow we say which patients are the ones  
3 that will be the indications, but they think it should  
4 be maybe stated which are the ones should not be  
5 considered. For example, patients that are responding  
6 to therapy, for example, it's not recommended for  
7 patients that are currently responding to levodopa.  
8 It's not for patients with dementia.

9 CHAIRPERSON CANADY: We have to be a  
10 little careful because almost all of these patients  
11 were responding to levodopa, but had some relatively  
12 negative effect of levodopa.

13 DR. ZAMORANO: Right.

14 CHAIRPERSON CANADY: So I'm not sure  
15 responsiveness, per se, is the right term.

16 DR. PIANTADOSI: We have criteria from the  
17 protocol. There were exclusion criteria in the  
18 protocol. They're not reflected though in the  
19 thoughts behind these questions and maybe it would be  
20 enough to point to those or state and crafted from the  
21 exclusionary criteria as contraindications.

22 CHAIRPERSON CANADY: Well, maybe we could

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1 DR. PIANTADOSI: I would add to that also  
2 that I'd be comfortable not voting on this personally,  
3 that I think the Agency has heard the discussion and  
4 the concern and knows what to do and I'm perfectly  
5 comfortable with that if people decided that they  
6 don't want to vote on it explicitly.

7 CHAIRPERSON CANADY: Dr. Hallett, what is  
8 your pleasure, it's your amendment?

9 DR. HALLETT: I would be happy to withdraw  
10 it as long as it's done.

11 (Laughter.)

12 CHAIRPERSON CANADY: Any additional  
13 amendments? Dr. Zamorano?

14 DR. ZAMORANO: I think we all have the  
15 concern that something like this gets approved. I  
16 think tomorrow every patient with Parkinson's disease  
17 is going to notify a surgeon to get bilateral  
18 stimulation. It should be labeled by the sponsor in  
19 some way contraindication or it's not advised in such  
20 and such patients.

21 CHAIRPERSON CANADY: This is the brass  
22 nuts part. You've got to say which patients.

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1 say the exclusion criteria of the protocol should be  
2 part of the labeling.

3 DR. MASSAQUOI: Question. Is it  
4 essential that things be made a contraindication  
5 versus a statement that says safety and/or  
6 effectiveness has not been established in a certain  
7 group?

8 CHAIRPERSON CANADY: Okay, that could be  
9 done.

10 DR. MASSAQUOI: In the situation where you  
11 don't know explicitly one or the other and there's not  
12 an overriding --

13 DR. ZAMORANO: Or it's not advisable in  
14 patients without saying it's a contraindication.

15 CHAIRPERSON CANADY: Since that group  
16 wasn't studied.

17 DR. ZAMORANO: Uh-huh.

18 CHAIRPERSON CANADY: We could say that  
19 safety was not established in this group and include  
20 the excluded population from the protocol. Is that  
21 acceptable to you or not? \*\*

22 DR. ZAMORANO: My concern is mostly with

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1 the patients that are currently in good -- that are  
2 well controlled with medical treatment, those patients  
3 because they will know that this exists, this  
4 bilateral stimulation, they will go and try to have  
5 this procedure and I think we need to provide some  
6 means that it doesn't happen. And we know it will  
7 happen between different colleagues, some get more  
8 excited about doing this bilateral stimulation and --

9 CHAIRPERSON CANADY: I think that that  
10 group is excluded by the statement in the first one  
11 which is only those patients who are advanced, and  
12 only those patients who are not adequately controlled  
13 was part of the original label. So I think we've  
14 covered that group.

15 DR. ZAMORANO: Yes. I think we covered  
16 it, but I don't know if we could add some second --

17 CHAIRPERSON CANADY: Is there additional  
18 people that you wish to include in that?

19 DR. EDMONDSON: No, I think we really do  
20 need a contraindication label that's clear. The  
21 exclusion criteria for the study is not, will not  
22 match one to one with what we really need. For

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1 example, patients over 75 are excluded in the study.  
2 We probably don't want to include an age  
3 contraindication or maybe we do want to say, I mean  
4 it's understood that Parkinson's occur in adults  
5 anyway, so an age limit or consideration is not  
6 necessary.

7 Secondary Parkinsonism, I think using  
8 levodopa responsive Parkinsonism is an important  
9 point, so excluding secondary Parkinson's patient  
10 would not be appropriate in the contraindication  
11 label.

12 CHAIRPERSON CANADY: Dr. Fessler?

13 DR. FESSLER: At this point all we really  
14 know is that this has been somewhat effective in  
15 patients with advanced Parkinson's who are responsive  
16 to levodopa, but are now losing their responsiveness.  
17 We don't know anything else and we really can't say  
18 it's contraindicated for conditions we don't know that  
19 it's contraindicated. That has to be a medical  
20 decision that has to be the doctor.

21 DR. EDMONDSON: However, when you put it  
22 in someone who is demented, quite demented -- so, you

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1 know, I think we still need some sort of guideline.

2 CHAIRPERSON CANADY: I need your  
3 recommendation.

4 DR. EDMONDSON: Number one, it is  
5 contraindicated in patients with dementia. Number  
6 one, that it is contraindicated in patients with  
7 coagulopathies. Number three, I don't know if you  
8 want to say -- I mean that would include folks with  
9 advanced hepatopathies and other potential  
10 coagulopathies. I think that's it.

11 CHAIRPERSON CANADY: A second? For that  
12 amendment that it would be contraindicated in dementia  
13 and in coagulopathy. Second?

14 [No second.]

15 I will entertain other amendments.

16 DR. WALKER: Can we change the wording to  
17 safety and efficacy has not been evaluated -- and done  
18 the same way.

19 CHAIRPERSON CANADY: A second for that?  
20 A second for the amendment, "safety and efficacy has  
21 not been demonstrated in dementia and in  
22 coagulopathy."

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1 DR. HALLETT: Well, coagulopathy --

2 CHAIRPERSON CANADY: Just dementia? What  
3 is your --

4 DR. HALLETT: There are certain exclusion  
5 criteria in this particular protocol. I mean  
6 coagulopathy and secondary drug-induced Parkinsonism,  
7 previous intracranial neurosurgical procedures, demand  
8 pacemakers, substance abuse, things like that which  
9 should be or could be considered exclusion criteria.

10 And then there are some other ones in  
11 which we just don't have the information such as age,  
12 so that one could say that safety and efficacy have  
13 not been demonstrated for patients older than age 75  
14 or perhaps some other things. But then there are  
15 other situations --

16 CHAIRPERSON CANADY: I need to know at  
17 this point in time those things.

18 (Laughter.)

19 This is no longer general conversation.

20 DR. HALLETT: Right.

21 CHAIRPERSON CANADY: So we can say the  
22 exclusion criteria of the protocol. And whatever you

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1 might wish to add to that or subtract from that.

2 DR. HALLETT: Okay, but I would think that  
3 we could say exclusion criteria are the ones that can  
4 be taken directly from the protocol.

5 CHAIRPERSON CANADY: So safety and  
6 efficacy has not been demonstrated under the excluded  
7 criteria. Is there a second for that amendment?

8 DR. PIANTADOSI: I second that, yes.

9 CHAIRPERSON CANADY: Conversation  
10 regarding this?

11 Call for the vote then. Dr. Walker?

12 DR. WALKER: Yes.

13 CHAIRPERSON CANADY: Dr. Zamorano?

14 DR. ZAMORANO: Yes.

15 CHAIRPERSON CANADY: Dr. Hallett?

16 DR. HALLETT: Yes.

17 CHAIRPERSON CANADY: Dr. Edmondson.

18 DR. EDMONDSON: Yes.

19 DR. NUWER: Yes.

20 DR. MASSAQUOI: Yes.

21 DR. FESSLER: No.

22 DR. PIANTADOSI: Yes.

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1 CHAIRPERSON CANADY: Additional  
2 amendments?

3 DR. PIANTADOSI: I have a question.

4 CHAIRPERSON CANADY: Yes sir.

5 DR. PIANTADOSI: Is the panel going to  
6 make any recommendations generically about safety?

7 CHAIRPERSON CANADY: If you would then so  
8 amend them, yes sir. Anything you want us to say  
9 needs to be said now.

10 DR. PIANTADOSI: Well, let me just raise  
11 the generic concern and see if one of my clinical  
12 colleagues can put it into better words. Many times  
13 labeling reflects the serious adverse events with  
14 approximate frequencies that they occur and I wonder  
15 out loud if anybody considers them to be clinically  
16 important enough that they should be put in the label  
17 and that the physicians contemplating the use of the  
18 device should be informed directly through the label  
19 about their frequency.

20 CHAIRPERSON CANADY: I need some wording.

21 DR. HALLETT: Could I just ask a question  
22 about that? For all of the other uses for DBS, has

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1 that already -- does that type of statement exist or  
2 not?

3 CHAIRPERSON CANADY: I can't answer that.  
4 I don't know.

5 DR. HALLETT: For example, for the  
6 indication for DBS of the thalamus for tremor, do we  
7 have that type of statement in the labeling?

8 CHAIRPERSON CANADY: Dr. Witten?

9 DR. WITTEN: I will just say that in  
10 general for PMA, in the label there's a description of  
11 -- the safety issues are described, but if there is  
12 some -- the safety issues from the study are  
13 described. But if there's some particular things that  
14 should be highlighted in some way, you know, those  
15 would be good to note. But otherwise, just in the  
16 general for any PMA --

17 CHAIRPERSON CANADY: That will happen.

18 DR. WITTEN: We note safety and there's a  
19 safety table in the label. But if there's any  
20 concerns about what needs to be said or what to do or  
21 suggestions like that, you could --

22 CHAIRPERSON CANADY: Obviously,

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1 hemiparesis is the major one.

2 DR. PIANTADOSI: That would satisfy my --

3 CHAIRPERSON CANADY: Other amendments.

4 Okay.

5 DR. ZAMORANO: I wonder if there is a way  
6 this panel can introduce an amendment related to the  
7 training of the physicians when to perform the  
8 procedure.

9 CHAIRPERSON CANADY: What is your  
10 amendment?

11 DR. ZAMORANO: I don't know how to phrase  
12 it, but basically, I mean related to the training of  
13 the -- need to be highly trained in this procedure,  
14 the physician.

15 CHAIRPERSON CANADY: I think it's an issue  
16 that we have -- that we need a specific statement as  
17 to how to add the two amendments.

18 DR. ZAMORANO: It could be a  
19 recommendation to the sponsor that to establish a  
20 mechanism for the training or to establish a criteria.

21 CHAIRPERSON CANADY: The concern I have  
22 regarding that is that it's not clear that that falls

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1 within the industry's purview to establish that is the  
2 concern in terms of how we go about establishing that.  
3 You might want to have a statement on the labeling  
4 regarding the concern that it be performed by  
5 physicians who are trained specifically in this  
6 procedure.

7 DR. ZAMORANO: Right.

8 CHAIRPERSON CANADY: I think that would be  
9 an amendment we could make.

10 DR. ZAMORANO: Maybe it could be related  
11 to the other one that we said, the potential  
12 complications of this procedure is so and so and so  
13 and that required a highly trained physician to  
14 perform this procedure.

15 CHAIRPERSON CANADY: Should we say that we  
16 would recommend specific training in this procedure be  
17 made available for physicians?

18 DR. ZAMORANO: That would be a good  
19 recommendation.

20 CHAIRPERSON CANADY: Would that be an  
21 acceptable version of y our amendment? Is there a  
22 second for that?

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1 DR. HALLETT: Could you say it again once  
2 more?

3 CHAIRPERSON CANADY: Specific training in  
4 this procedure should be made available for  
5 physicians.

6 DR. HALLETT: Could we say that specific  
7 training in the procedure is recommended for  
8 physicians?

9 CHAIRPERSON CANADY: Yes, we surely can.

10 DR. WALKER: I'll second that.

11 CHAIRPERSON CANADY: Second?

12 DR. WALKER: Yes.

13 CHAIRPERSON CANADY: Any more comment?  
14 Vote. Dr. Walker?

15 DR. WALKER: Yes.

16 CHAIRPERSON CANADY: Dr. Zamarano?

17 DR. ZAMORANO: Yes.

18 DR. HALLETT: Yes.

19 DR. EDMONDSON: Yes.

20 DR. NUWER: Yes.

21 DR. MASSAQUOI: Yes.

22 DR. PIANTADOSI: Yes.

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1 CHAIRPERSON CANADY: Other comments,  
2 amendments?

3 DR. MASSAQUOI: One amendment. Third from  
4 the last item. Regarding the increase in duration and  
5 quality of on time and decreases the duration of off  
6 time without mentioning the severity of off time  
7 unless -- I didn't --

8 CHAIRPERSON CANADY: You wish to exclude  
9 severity?

10 DR. MASSAQUOI: Yes, severity of off time.

11 CHAIRPERSON CANADY: Is there a second?

12 DR. MASSAQUOI: I just don't recall the  
13 data off hand. Maybe if someone could remind me. I  
14 just didn't recall that as being established that  
15 during the periods when people were off that they were  
16 less severe --

17 DR. NUWER: I thought that was  
18 established. It was part of the data that was  
19 presented.

20 The severity in the off was not that much  
21 different from the on before implanted.

22 DR. MASSAQUOI: Okay, fine, I'll withdraw.

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1 Thank you.

2 CHAIRPERSON CANADY: You withdraw that.

3 Any other amendments?

4 Okay, now I'd like to take a vote on the  
5 major motion which is approvable with conditions. The  
6 conditions are the conditions that we have voted on.  
7 This would also be your opportunity to make a comment  
8 regarding the entire -- we should vote first and then  
9 the reasons?

10 CHAIRPERSON CANADY: Dr. Walker?

11 DR. WALKER: I'll vote yes. Thirty  
12 seconds of comment, running a multicenter clinical  
13 study of 22 bright and innovative principal  
14 investigators, especially neurosurgeons is probably  
15 something like herding cats.

16 CHAIRPERSON CANADY: Neurosurgeons, of  
17 course, take offense to this.

18 DR. WALKER: I think the sponsor did a  
19 good job in this and I think that by approving this  
20 today the panel is making a big contribution to what's  
21 available to Parkinson's <sup>\*\*</sup> patients.

22 CHAIRPERSON CANADY: Dr. Zamarano?

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1 DR. ZAMORANO: Yes, a very brief comment.  
2 I think this is an excellent possibility to offer to  
3 some of the patients and I think with the condition  
4 that we have outlined it makes good step, the  
5 approval.

6 CHAIRPERSON CANADY: Dr. Hallett.

7 DR. HALLETT: I vote yes. I think the  
8 most important reason is the prolongation of the on  
9 effect which gives rise to a better lifestyle for the  
10 patients.

11 CHAIRPERSON CANADY: Dr. Edmondson?

12 DR. EDMONDSON: I vote yes and I'll say  
13 ditto to my predecessors.

14 CHAIRPERSON CANADY: Dr. Nuwer?

15 DR. NUWER: I vote yes and add that I  
16 think that the improvement in the patients' clinical  
17 status outweighs the methodological flaws in the  
18 matter before us.

19 CHAIRPERSON CANADY: Dr. Massaquoi?

20 DR. MASSAQUOI: I vote yes and I'll just  
21 ditto and also say that it does seem that despite the  
22 methodological problems, there was an incredible

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1 amount of work that was done and it was headed all in  
2 the right direction, I think.

3 CHAIRPERSON CANADY: Dr. Piantadosi?

4 DR. PIANTADOSI: I'll vote yes with no  
5 additional comment. Thank you.

6 CHAIRPERSON CANADY: Then the motion  
7 passes with conditions as outlined. I believe that's  
8 the end of the meeting.

9 Any other comments the panelists would  
10 like to make?

11 DR. COHEN: Yes, I'd like to make a  
12 comment as a patient. I'm pleased with the outcome  
13 and that I'm glad we stuck close to the data and I'm  
14 glad that we approved this treatment.

15 CHAIRPERSON CANADY: Dr. Witten?

16 DR. WITTEN: I'd like to thank the panel  
17 and everyone else who participated today.

18 (Applause.)

19 CHAIRPERSON CANADY: The meeting is  
20 adjourned.

21 (Whereupon, at 5:39 p.m., the meeting was  
22 concluded.)

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CERTIFICATE


This is to certify that the foregoing transcript in the  
matter of:                   Neurological Devices Panel of the  
                                  Medical Devices Advisory Committee

Before:                   DHHS/FDA

Date:                    March 31, 2000

Place:                   Rockville, MD

represents the full and complete proceedings of the  
aforementioned matter, as reported and reduced to  
typewriting.

  
A handwritten signature in dark ink, appearing to be "J. M. [unclear]", is written over a horizontal line.